



U.S. Patent No. 6,893,636
Attorney Docket No. 037003-0275470

Wyc

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. PATENT NUMBER 6,893,636

Issued: May 17, 2005

Mitchell REFF et al.

Group Art Unit: 1644

Application No. 09/019,441

Examiner: Phuong N. Huynh

Filed: February 5, 1998

Title: GAMMA-1 AND GAMMA-3 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES
AND USE THEREOF AS THERAPEUTICS

* * * * *

REQUEST FOR CERTIFICATE OF CORRECTION

PURSUANT TO 37 C.F.R. § 1.323

ATTN: Certificate of Correction Branch

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Certificate

JUN 13 2005

of Correction

Sir:

Pursuant to 37 C.F.R. § 1.323, patentee respectfully requests that a Certificate of Correction be issued in the above-identified patent to correct the sequence listing. Specifically, the substitute sequence listing filed in the United States Patent and Trademark (USPTO) on April 28, 2004, is not included in the issued patent. A Form PTO/SB/44 is attached, which directs replacement of the entire sequence listing of the issued patent with the substitute sequence listing filed on April 28, 2004. The proposed corrections do not constitute new matter or require reexamination.

The official action mailed January 16, 2004, included a third notice to comply with sequence listing requirements. In response to the notice to comply, a substitute sequence listing was filed April 28, 2004, along with an amendment to employ sequence modifiers consistent with the substitute sequence listing. The amendments to the specification appear in the issued patent, however, the substitute sequence listing is omitted. A copy of the complete submission of April 28, 2004, is enclosed, including a date-stamped cover sheet indicating receipt by the USPTO. Essentially,

JUN 14 2005

the Patent Office, in error, printed the above-reference patent with an incorrect, prior version of the specification.

Based on the foregoing, applicants believe that issuance of the patent with an incorrect sequence listing is the result of error on the part of the USPTO. Although the applicant believes no fee is due for processing of this request, should the Patent Office determine otherwise, such fees (for the processing of this request) may be charged to Deposit Account No. 33975 under Order No. 037003-027540.

Respectfully submitted,

PILLSBURY WINTHROP SHAW PITTMAN LLP

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McLean, VA 22102
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Date: June 9, 2005

TAC/JBM

**UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION**

PATENT NO : 6893636

DATED : May 17, 2005

INVENTOR(S) :
MITCHELL E REFF, ET AL

It is certified that error appears in the above-identified patent and that said Letters Patent
is hereby corrected as shown below:

In Sequence Listing,
replace "Sequence Listing"
with --attached Sequence Listing--.

MAILING ADDRESS OF SENDER:

PILLSBURY WINTHROP SHAW PITTMAN LLP
P.O. Box 10500
McLean, VA 22102

PATENT NO. 6893636

No. of additional copies



This collection of information is required by 37 CFR 1.322, 1.323, and 1.324. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1.0 hour to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Attention Certificate of Corrections Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

JUN 14 2005



U.S. Application No. 09/019,441
Attorney Ref. No. 037003-0275470

SEQUENCE LISTING

<110> REFF, MITCHELL E.
KLOETZER, WILLIAM S.
NAKAMURA, TAKEHIKO

<120> GAMMA-1 AND GAMMA-3 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES AND USE
THEREOF AS THERAPEUTICS

<130> 037003-0275470

<140> 09/019,441

<141> 1998-02-05

<150> 08/803,085

<151> 1997-02-20

<160> 39

<170> PatentIn Ver. 2.1

<210> 1

<211> 390

<212> DNA

<213> Artificial Sequence

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World Monkey (macaque); leader sequence is an artificial sequence to
facilitate cloning

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<222> (1)..(57)

<223> leader sequence

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<222> (1)..(390)

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tcc tgg gct cag tct gcc ccg act cag cct ccc tct gtg tct ggg tct	96
Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser	
-1 1 5 10	

cct gga cag tcg gtc acc atc tcc tgc act gga acc agc gat gac gtt	144
Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val	
15 20 25	

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ggt ggt tat aac tat gtc tcc tgg tac caa cac cac cca ggc aaa gcc 192
Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
30 35 40 45

ccc aaa ctc atg att tat gat gtc gct aag cgg gcc tca ggg gtc tct 240
Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
50 55 60

gat cgc ttc tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc 288
Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
65 70 75

tct ggg ctc cag gct gag gac gag gct gat tat tac tgt tgt tca tat 336
Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
80 85 90

aca acc agt agc act ttg tta ttc gga aga ggg acc cgg ttg acc gtc 384
Thr Thr Ser Ser Thr Leu Leu Phe Gly Arg Gly Thr Arg Leu Thr Val
95 100 105

cta ggt 390
Leu Gly
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Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser
-1 1 5 10

Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val
15 20 25

Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
30 35 40 45

Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
50 55 60

Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
65 70 75

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
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<210> 3
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<223> leader sequence

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<222> (58)..(423)

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<222> (1)..(423)

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-15 -10 -5	
gtc ctg tcc cag ctg cag ctg cag gag tgc ggc cca gga gtg gtg aag	96
Val Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys	
-1 1 5 10	
cct tgc gag acc ctg tcc ctc acc tgc gct gtc tct ggt ggc tct gtc	144
Pro Ser Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val	
15 20 25	
agc agt agt aac tgg tgg acc tgg atc cgc cag ccc cca ggg aag gga	192
Ser Ser Ser Asn Trp Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly	
30 35 40 45	
ctg gag tgg att gga cgt atc tct ggt agt ggt ggg gcc acc aac tac	240
Leu Glu Trp Ile Gly Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr	
50 55 60	
aac ccg tcc ctc aag agt cga gtc atc att tca caa gac acg tcc aag	288
Asn Pro Ser Leu Lys Ser Arg Val Ile Ile Ser Gln Asp Thr Ser Lys	
65 70 75	
aac cag ttc tcc ctg aac ctg aac tct gtg acc gcc gcg gac acg gcc	336
Asn Gln Phe Ser Leu Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala	
80 85 90	
gtg tat tac tgt gcc aga gat tgg gcc caa ata gct gga aca acg cta	384
Val Tyr Tyr Cys Ala Arg Asp Trp Ala Gln Ile Ala Gly Thr Thr Leu	
95 100 105	

ggc ttc tgg ggc cag gga gtc ctg gtc acc gtc tcc tca
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

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<210> 4
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-15 -10 -5
Val Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys
-1 1 5 10
Pro Ser Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val
15 20 25
Ser Ser Ser Asn Trp Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly
30 35 40 45
Leu Glu Trp Ile Gly Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr
50 55 60
Asn Pro Ser Leu Lys Ser Arg Val Ile Ile Ser Gln Asp Thr Ser Lys
65 70 75
Asn Gln Phe Ser Leu Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala
80 85 90
Val Tyr Tyr Cys Ala Arg Asp Trp Ala Gln Ile Ala Gly Thr Thr Leu
95 100 105
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

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<223> leader sequence

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-20 -15 -10	
ctc cca ggt gcc aga tgt gac atc cag atg acc cag tct cca tct tcc	96
Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser	
-5 -1 1 5 10	
ctg tct gca tct gta ggg gac aga gtc acc atc act tgc agg gca agt	144
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser	
15 20 25	
cag gac att agg tat tat tta aat tgg tat cag cag aaa cca gga aaa	192
Gln Asp Ile Arg Tyr Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys	
30 35 40	
gct cct aag ctc ctg atc tat gtt gca tcc agt ttg caa agt ggg gtc	240
Ala Pro Lys Leu Leu Ile Tyr Val Ala Ser Ser Leu Gln Ser Gly Val	
45 50 55	
cca tca agg ttc agc ggc agt gga tct ggg aca gag ttc act ctc acc	288
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr	
60 65 70	
gtc agc agc ctg cag cct gaa gat ttt gcg act tat tac tgt cta cag	336
Val Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln	
75 80 85 90	
gtt tat agt acc cct cgg acg ttc ggc caa ggg acc aag gtg gaa atc	384
Val Tyr Ser Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile	
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Lys	

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Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser

-5	-1	1		5		10									
Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser
				15					20					25	
Gln	Asp	Ile	Arg	Tyr	Tyr	Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys
			30					35					40		
Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Val	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val
		45					50					55			
Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr
	60					65					70				
Val	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Leu	Gln
	75				80					85					90
Val	Tyr	Ser	Thr	Pro	Arg	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile
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Lys

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				-15				-10						-5		
gtc	cag	tgt	gag	gtg	cag	ctg	gtg	gag	tct	ggg	ggc	ggc	ttg	gca	aag	96
Val	Gln	Cys	Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Ala	Lys	
	-1	1					5					10				
cct	ggg	ggg	tcc	ctg	aga	ctc	tcc	tgc	gca	gcc	tcc	ggg	ttc	agg	ttc	144
Pro	Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Arg	Phe	
	15					20					25					

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acc ttc aat aac tac tac atg gac tgg gtc cgc cag gct cca ggg cag 192
Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
 30                      35                      40                      45

ggg ctg gag tgg gtc tca cgt att agt agt agt ggt gat ccc aca tgg 240
Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
                      50                      55                      60

tac gca gac tcc gtg aag ggc aga ttc acc atc tcc aga gag aac gcc 288
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
                      65                      70                      75

aac aac aca ctg ttt ctt caa atg aac agc ctg aga gct gag gac acg 336
Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                      80                      85                      90

gct gtc tat tac tgt gcg agc ttg act aca ggg tct gac tcc tgg ggc 384
Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
 95                      100                      105

cag gga gtc ctg gtc acc gtc tcc tca 411
Gln Gly Val Leu Val Thr Val Ser Ser
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Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys
      -1    1                      5                      10

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe
      15                      20                      25

Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
      30                      35                      40                      45

Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
      50                      55                      60

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
      65                      70                      75

Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
      80                      85                      90

Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
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Gln Gly Val Leu Val Thr Val Ser Ser
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<211> 34

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<210> 35

<211> 20

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<210> 36

<211> 30

<212> DNA

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<400> 39

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SEQUENCE LISTING

<110> REFF, MITCHELL E.
KLOETZER, WILLIAM S.
NAKAMURA, TAKEHIKO

<120> GAMMA-1 AND GAMMA-3 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES AND USE
THEREOF AS THERAPEUTICS

<130> 037003-0275470

<140> 09/019,441

<141> 1998-02-05

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World Monkey (macaque); leader sequence is an artificial sequence to
facilitate cloning

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<400> 1

atg gcc tgg act ctg ctc ctc gtc acc ctc ctc act cag ggc aca gga	48
Met Ala Trp Thr Leu Leu Leu Val Thr Leu Leu Thr Gln Gly Thr Gly	
-15 -10 -5	

tcc tgg gct cag tct gcc ccg act cag cct ccc tct gtg tct ggg tct	96
Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser	
-1 1 5 10	

cct gga cag tcg gtc acc atc tcc tgc act gga acc agc gat gac gtt	144
Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val	
15 20 25	

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ggt ggt tat aac tat gtc tcc tgg tac caa cac cac cca ggc aaa gcc 192
Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
 30          35          40          45

ccc aaa ctc atg att tat gat gtc gct aag cgg gcc tca ggg gtc tct 240
Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
          50          55          60

gat cgc ttc tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc 288
Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
          65          70          75

tct ggg ctc cag gct gag gac gag gct gat tat tac tgt tgt tca tat 336
Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
          80          85          90

aca acc agt agc act ttg tta ttc gga aga ggg acc cgg ttg acc gtc 384
Thr Thr Ser Ser Thr Leu Leu Phe Gly Arg Gly Thr Arg Leu Thr Val
          95          100          105

cta ggt
Leu Gly
110

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<210> 2
<211> 130
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<400> 2

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Met Ala Trp Thr Leu Leu Leu Val Thr Leu Leu Thr Gln Gly Thr Gly
          -15          -10          -5

Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser
          -1    1          5          10

Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val
          15          20          25

Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
          30          35          40          45

Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
          50          55          60

Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
          65          70          75

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
          80          85          90

Thr Thr Ser Ser Thr Leu Leu Phe Gly Arg Gly Thr Arg Leu Thr Val
          95          100          105

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Leu Gly
110

<210> 3
<211> 423
<212> DNA
<213> Artificial Sequence

<220>
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<220>
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<222> (1)..(57)
<223> leader sequence

<220>
<221> mat_peptide
<222> (58)..(423)

<220>
<221> CDS
<222> (1)..(423)

<400> 3

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Met	Lys	His	Leu	Trp	Phe	Phe	Leu	Leu	Leu	Val	Ala	Ala	Pro	Arg	Trp	
			-15						-10					-5		
gtc	ctg	tcc	cag	ctg	cag	ctg	cag	gag	tcg	ggc	cca	gga	gtg	gtg	aag	96
Val	Leu	Ser	Gln	Leu	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Val	Val	Lys	
	-1	1				5						10				
cct	tcg	gag	acc	ctg	tcc	ctc	acc	tgc	gct	gtc	tct	ggt	ggc	tct	gtc	144
Pro	Ser	Glu	Thr	Leu	Ser	Leu	Thr	Cys	Ala	Val	Ser	Gly	Gly	Ser	Val	
	15					20					25					
agc	agt	agt	aac	tgg	tgg	acc	tgg	atc	cgc	cag	ccc	cca	ggg	aag	gga	192
Ser	Ser	Ser	Asn	Trp	Trp	Thr	Trp	Ile	Arg	Gln	Pro	Pro	Gly	Lys	Gly	
30				35				40						45		
ctg	gag	tgg	att	gga	cgt	atc	tct	ggt	agt	ggt	ggg	gcc	acc	aac	tac	240
Leu	Glu	Trp	Ile	Gly	Arg	Ile	Ser	Gly	Ser	Gly	Gly	Ala	Thr	Asn	Tyr	
			50					55						60		
aac	ccg	tcc	ctc	aag	agt	cga	gtc	atc	att	tca	caa	gac	acg	tcc	aag	288
Asn	Pro	Ser	Leu	Lys	Ser	Arg	Val	Ile	Ile	Ser	Gln	Asp	Thr	Ser	Lys	
			65				70					75				
aac	cag	ttc	tcc	ctg	aac	ctg	aac	tct	gtg	acc	gcc	gcg	gac	acg	gcc	336
Asn	Gln	Phe	Ser	Leu	Asn	Leu	Asn	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	
	80					85					90					
gtg	tat	tac	tgt	gcc	aga	gat	tgg	gcc	caa	ata	gct	gga	aca	acg	cta	384
Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Trp	Ala	Gln	Ile	Ala	Gly	Thr	Thr	Leu	
	95					100					105					

ggc ttc tgg ggc cag gga gtc ctg gtc acc gtc tcc tca
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

423

<210> 4
<211> 141
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<400> 4

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
-15 -10 -5
Val Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys
-1 1 5 10
Pro Ser Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val
15 20 25
Ser Ser Ser Asn Trp Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly
30 35 40 45
Leu Glu Trp Ile Gly Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr
50 55 60
Asn Pro Ser Leu Lys Ser Arg Val Ile Ile Ser Gln Asp Thr Ser Lys
65 70 75
Asn Gln Phe Ser Leu Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala
80 85 90
Val Tyr Tyr Cys Ala Arg Asp Trp Ala Gln Ile Ala Gly Thr Thr Leu
95 100 105
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

<210> 5
<211> 387
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<220>
<221> misc_feature
<222> (1)..(66)
<223> leader sequence

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<221> mat_peptide
<222> (67)..(387)

<220>
<221> CDS
<222> (1)..(387)

<400> 5

atg gac atg agg gtc ccc gct cag ctc ctg ggg ctc ctt ctg ctc tgg	48
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp	
-20 -15 -10	
ctc cca ggt gcc aga tgt gac atc cag atg acc cag tct cca tct tcc	96
Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser	
-5 -1 1 5 10	
ctg tct gca tct gta ggg gac aga gtc acc atc act tgc agg gca agt	144
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser	
15 20 25	
cag gac att agg tat tat tta aat tgg tat cag cag aaa cca gga aaa	192
Gln Asp Ile Arg Tyr Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys	
30 35 40	
gct cct aag ctc ctg atc tat gtt gca tcc agt ttg caa agt ggg gtc	240
Ala Pro Lys Leu Leu Ile Tyr Val Ala Ser Ser Leu Gln Ser Gly Val	
45 50 55	
cca tca agg ttc agc ggc agt gga tct ggg aca gag ttc act ctc acc	288
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr	
60 65 70	
gtc agc agc ctg cag cct gaa gat ttt gcg act tat tac tgt cta cag	336
Val Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln	
75 80 85 90	
gtt tat agt acc cct cgg acg ttc ggc caa ggg acc aag gtg gaa atc	384
Val Tyr Ser Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile	
95 100 105	
aaa	387
Lys	

<210> 6
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<400> 6

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
-20 -15 -10
Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser

-5	-1	1	5	10
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser	15	20	25	
Gln Asp Ile Arg Tyr Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys	30	35	40	
Ala Pro Lys Leu Leu Ile Tyr Val Ala Ser Ser Leu Gln Ser Gly Val	45	50	55	
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr	60	65	70	
Val Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln	75	80	85	90
Val Tyr Ser Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile	95	100	105	

Lys

<210> 7
<211> 411
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<220>
<221> misc_feature
<222> (1)..(57)
<223> leader sequence

<220>
<221> mat_peptide
<222> (58)..(411)

<220>
<221> CDS
<222> (1)..(411)

<400> 7

atg gag ttt ggg ctg agc tgg gtt ttc ctt gtt cct ctt ttg aaa ggt	48
Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Pro Leu Leu Lys Gly	
-15 -10 -5	
gtc cag tgt gag gtg cag ctg gtg gag tct ggg ggc ggc ttg gca aag	96
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys	
-1 1 5 10	
cct ggg ggg tcc ctg aga ctc tcc tgc gca gcc tcc ggg ttc agg ttc	144
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe	
15 20 25	

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acc ttc aat aac tac tac atg gac tgg gtc cgc cag gct cca ggg cag 192
Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
 30                      35                      40                      45

ggg ctg gag tgg gtc tca cgt att agt agt agt ggt gat ccc aca tgg 240
Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
                      50                      55                      60

tac gca gac tcc gtg aag ggc aga ttc acc atc tcc aga gag aac gcc 288
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
                      65                      70                      75

aac aac aca ctg ttt ctt caa atg aac agc ctg aga gct gag gac acg 336
Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
                      80                      85                      90

gct gtc tat tac tgt gcg agc ttg act aca ggg tct gac tcc tgg ggc 384
Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
 95                      100                      105

cag gga gtc ctg gtc acc gtc tcc tca 411
Gln Gly Val Leu Val Thr Val Ser Ser
110                      115

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<210> 8
<211> 137
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<400> 8

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Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Pro Leu Leu Lys Gly
      -15                      -10                      -5

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys
      -1   1                      5                      10

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe
  15                      20                      25

Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
 30                      35                      40                      45

Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
 50                      55                      60

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
 65                      70                      75

Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
 80                      85                      90

Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
 95                      100                      105

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Gln Gly Val Leu Val Thr Val Ser Ser
110 115

<210> 9
<211> 41
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<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 9
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<210> 10
<211> 35
<212> DNA
<213> Artificial Sequence

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<400> 10
atcacagatc tctcaccatg aggctccctg ctgag 35

<210> 11
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 11
atcacagatc tctcaccatg gaarccccag ckag 35

<210> 12
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 12
atcacagatc tctcaccatg gtgttgacaga cccaggtc 38

<210> 13
<211> 32
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 13

ggtgcagcca ccgtagcttt gatytcasc tt

32

<210> 14

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 14

atcacagatc tctcaccatg rcttgstccc ctct

34

<210> 15

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 15

atcacagatc tctcaccatg gcctggrctc ygct

34

<210> 16

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 16

atcacagatc tctcaccatg gcmgtggaycc ctctc

35

<210> 17

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 17

cttgggctga cctaggacgg t

21

<210> 18

<211> 30

<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 18

gcgactaagt cgaccatgga ctggacctgg

30

<210> 19
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 19

gcgactaagt cgaccatgaa acacctgtgg

30

<210> 20
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 20

gcgactaagt cgaccatgga gtttgggctg agc

33

<210> 21
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 21

gcgactaagt cgaccatggg gtcaaccgcc atc

33

<210> 22
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
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<400> 22

gcgactaagt cgaccatgtc tgtctccttc etc

33

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<210> 23
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 23

gccaggggga agaccgatgg gcccttggtg ctagctgagg agacgg

46

<210> 24
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 24

gatgggccct tgggtgctagc tgaggagacg g

31

<210> 25
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 25

ggtgctagct gaggagacgg tgaccaggac tccctggccc cagaagccta g

51

<210> 26
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 26

atttaggtga cactata

17

<210> 27
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 27

gttttcccag tcacga

16

<210> 28

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 28

atatacgact cactataggg

20

<210> 29

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 29

ccgtcagatc gcctggagac gcca

24

<210> 30

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 30

gcagttccag atttcaactg

20

<210> 31

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 31

ccaggccact gtcacggctt c

21

<210> 32

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 32

cagagctggg tacgtcctca

20

<210> 33

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 33

gccccagag gtgctcttg

20

<210> 34

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 34

acacagacc gtcgacatgg

20

<210> 35

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 35

gctctcggag gtgctcctgg

20

<210> 36

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 36

acagaccgt cgaccatgga gtttgggctg

30

<210> 37
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 37

ccccttggtg ctagctgagg agacggt

27

<210> 38
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 38

agagagaacg ccaagaacac actgttt

27

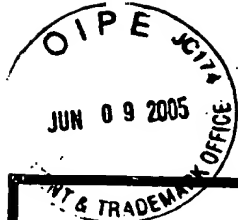
<210> 39
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 39

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27



13
COPY

RECEIPT FROM PTO FOR INDICATED ITEMS

(Do NOT Use for New or Continuing Applications of Any Kind)
Use 2 postcards for all New Applns. (cont/Div/CIP, too)
Use this sheet when filing CPA

Appln. No: 09/019,441	Atty: Thomas A. Cawley, Jr./JBM/NTBerg
First Inventor: REFF	Date: April 28, 2004
	Matter No: 0275470
	Client No: 037003

ENCLOSED:

- ☒ Amendment
- ☒ Copy of Notice to Comply with Requirements for Patent Applications Containing Nucleotide and/or Amino Acid Sequences
- ☒ Substitute Sequence Listing (Paper Copy and CRF Copy)
- ☒ Statement Pursuant to 37 C.F.R. 1.821(f)
- ☒ Petition for One-Month Extension of Time

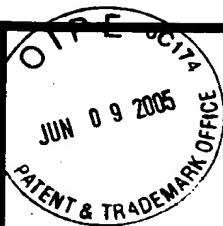
\$110.00 Amount Requested be Charged to our Dep. Acct. No. 03-3975

Current DUE DATE:

May 16, 2004

(Submit Single Copy Only)





RECEIPT FROM PTO FOR INDICATED ITEMS

(Do NOT Use for New or Continuing Applications of Any Kind)
Use 2 postcards for all New Applns. (cont/Div/CIP, too)
Use this sheet when filing CPA

Appln. No: 09/019,441	Atty: Thomas A. Cawley, Jr./JBM/NTBerg
First Inventor: REFF	Date: April 28, 2004
	Matter No: 0275470
	Client No: 037003

ENCLOSED:

- ☒ Amendment
- ☒ Copy of Notice to Comply with Requirements for Patent Applications Containing Nucleotide and/or Amino Acid Sequences
- ☒ Substitute Sequence Listing (Paper Copy and CRF Copy)
- ☒ Statement Pursuant to 37 C.F.R. 1.821(f)
- ☒ Petition for One-Month Extension of Time

\$110.00 Amount Requested be Charged to our Dep. Acct. No. 03-3975

Current DUE DATE:

May 16, 2004

(Submit Single Copy Only)

U.S. Patent Appl. No. 09/019,441
Attorney Docket No. 037003-0275470



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION OF

Mitchell R. REFF et al.

Group Art Unit: 1644

Application Serial No. 09/019,441

Examiner: Phuong N. Huynh

Filed: February 5, 1998

Title: GAMMA-1 AND GAMMA-3 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES
AND USE THEREOF AS THERAPEUTICS

* * * * *

AMENDMENT PURSUANT TO 37 C.F.R. § 1.111

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is in response to the official action dated January 16, 2004, wherein the claims were rejected under 35 U.S.C. § 112, second paragraph. The applicants traverse the outstanding rejections in view of the following amendments and remarks. This response is timely filed with the enclosed petition for a one-month extension of time and payment of the requisite fee.

20 23
Gln Ser Val Thr Ile Ser Cys
CAG TCG GTC ACC ATC TCC TGC (SEQ ID NO: 1 – bases 58-123)

Please amend the captioned section beginning at page 44, line 23, as follows:

CDR 1

24 27 27A 27B 27C 28 34
Thr Gly Thr Ser Asp Asp Val Gly Gly Tyr Asn Tyr Val Ser
ACT GGA ACC AGC GAT GAC GTT GGT GGT TAT AAC TAT GTC TCC
(SEQ ID NO: 1 – bases 124-165)

Please amend the captioned section beginning at page 44, line 27, as follows:

Framework 2

35 40 49
Trp Tyr Gln His His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr
TGG TAC CAA CAC CAC CCA GGC AAA GCC CCC AAA CTC ATG ATT TAT
(SEQ ID NO: 1 – bases 166-210)

Please amend the captioned section beginning at page 45, line 1, as follows:

CDR2

50 56
Asp Val Ala Lys Arg Ala Ser
GAT GTC GCT AAG CGG GCC TCA (SEQ ID NO: 1 – bases 211-231)

Please amend the captioned section beginning at page 45, line 5, as follows:

Framework 3

57 60 70
Gly Val Ser Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala
GGG GTC TCT GAT CGC TTC TCT GGC TCC AAG TCT GGC AAC ACG GCC
80
Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr
TCC CTG ACC ATC TCT GGG CTC CAG GCT GAG GAC GAG GCT GAT TAT
88
Tyr Cys
TAC TGT (SEQ ID NO: 1 – bases 232-327)

Please amend the captioned section beginning at page 45, line 15, as follows:

CDR 3

89	90							95	95A	96	97
Cys	Ser	Tyr	Thr	Thr	Ser	Ser	Thr	Leu	Leu		
TGT	TCA	TAT	ACA	ACC	AGT	AGC	ACT	TTG	TTA	<u>(SEQ ID NO: 1 – bases 328-357)</u>	

Please amend the captioned section beginning at page 45, line 19, as follows:

Framework 4

98		100								106	106A	107
Phe	Gly	Arg	Gly	Thr	Arg	Leu	Thr	Val	Leu	Gly		
TTC	GGA	AGA	GGG	ACC	CGG	TTG	ACC	GTC	CTA	GGT	<u>(SEQ ID NO: 1 – bases 358-390)</u>	

Please amend the captioned section beginning at page 45, line 23, as follows:

2) Cloning the heavy chain variable domain of primate monoclonal anti-human CD23 antibody 6G5 by PCR

The first PCR amplification of the heavy chain variable domain from cDNA of primate monoclonal antibody 6G5 was performed by using the set of early leader sequence primers described supra and the 3' J region primer GE244 (SEQ ID NO: 23). These primers are in Tables 1-3 (SEQ ID NOs: 9-25) infra. This reaction resulted in a 350 base PCR product. This 350 base product (purified as described supra), was digested with Nhe I and Sal I, and ligated into N5LG1 and digested with the same endonucleases in the first PCR amplification. The resultant ligation mixture was transformed into host cells using the same techniques for cloning the light chain. Plasmid N5LG1 containing the 350 base PCR product was then isolated and sequenced (using sequencing primers 266 (SEQ ID NO: 32) and 268) (SEQ ID NO: 33). (These Sequencing primers are set forth in Table 4 (SEQ ID NOs: 26-35).)

Please amend the paragraph beginning at page 46, line 15, as follows:

A second independent PCR reaction was conducted to amplify and isolate the heavy chain variable domain of primate monoclonal antibody 6G5 using a 5' early leader sequence primer for family 1 (MB1503) (SEQ ID NO: 18) and a 3' J' region primer GE244 (SEQ ID NO: 23). (These primers are also contained in Tables 1-3 (SEQ ID NOs: 9-25)). The resultant

PCR product was then cloned into the NSLG1 using the same techniques described supra. Its sequence was found to be identical to the first PCR product.

Please amend the paragraph beginning at page 46, line 24, as follows:

Therefore, in order to clone the whole heavy variable domain of 6G5 including the missing 5' terminus a new longer 3' primer (MB1533) (SEQ ID NO: 25) which included the CDR3 and framework 4 regions of the 6G5 heavy variable chain was then used in a third independent PCR reaction with the family 1 5' primer (MB1503) (SEQ ID NO: 18). (These primers are also contained in Tables 1-3 (SEQ ID NOs: 9-25).)

Please amend the captioned section beginning at page 47, line 6, as follows:

A fourth independent PCR was performed using the same primers as the third PCR amplification. This resulted in a PCR product which was isolated and cloned into the TA vector as described previously. The sequence of the fourth independent PCR product was found to be identical to that obtained in the third PCR amplification. This sequence, which comprises the heavy chain variable domain of primate monoclonal anti-human CD23 antibody 6G5, is presented below (~~SEQ ID NO: 2~~) as an alignment of the nucleotide sequence (SEQ ID NO: 3) and the encoded amino acid sequence (SEQ ID NO:4).

Please amend the captioned section beginning at page 47, line 15, as follows:

**Heavy chain variable region of primate monoclonal
antibody anti-human CD23 6G5**

Leader

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg
ATG AAA CAC CTG TGG TTC TTC CTC CTC CTG GTG GCA GCT CCC AGA

-1

Trp Val Leu Ser

TGG GTC CTG TCC (SEQ ID NO: 3 – bases 1-57) -

Please amend the captioned section beginning at page 47, line 23, as follows:

Mature Protein (Numbering is Kabat)

Framework 1

1 10
Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys Pro Ser
CAG CTG CAG CTG CAG GAG TCG GGC CCA GGA GTG GTG AAG CCT TCG
20 30
Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val Ser
GAG ACC CTG TCC CTC ACC TGC GCT GTC TCT GGT GGC TCT GTC AGC
(SEQ ID NO: 3 – bases 58-147)

Please amend the captioned section beginning at page 48, line 1, as follows:

CDR 1

31 35 35a
Ser Ser Asn Trp Trp Thr
AGT AGT AAC TGG TGG ACC (SEQ ID NO: 3 – bases 148-165)

Please amend the captioned section beginning at page 48, line 5, as follows:

Framework 2

36 40 49
Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
TGG ATC CGC CAG CCC CCA GGG AAG GGA CTG GAG TGG ATT GGA
(SEQ ID NO: 3 – bases 166-207)

Please amend the captioned section beginning at page 48, line 16, as follows:

CDR2

50 52 52A 53 60
Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr Asn Pro Ser Leu
CGT ATC TCT GGT AGT GGT GGG GCC ACC AAC TAC AAC CCG TCC CTC
65
Lys Ser
AAG AGT (SEQ ID NO: 3 – bases 208-258)

Please amend the captioned section beginning at page 48, line 16, as follows:

Framework 3

66 70 80
Arg Val Ile Ile Ser Gln Asp Thr Ser Lys Asn Gln Phe Ser Leu
CGA GTC ATC ATT TCA CAA GAC ACG TCC AAG AAC CAG TTC TCC CTG

82 82a 82b 82c 83 90
Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
AAC CTG AAC TCT GTG ACC GCC GCG GAC ACG GCC GTG TAT TAC TGT
94
Ala Arg
GCC AGA (SEQ ID NO: 3 – bases 259-354)

Please amend the captioned section beginning at page 48, line 26, as follows:

CDR 3

95 100 100a 100b 100c 100d 101 102
Asp Trp Ala Gln Ile Ala Gly Thr Thr Leu Gly Phe
GAT TGG GCC CAA ATA GCT GGA ACA ACG CTA GGC TTC
(SEQ ID NO: 3 – bases 355-390)

Please amend the captioned section beginning at page 49, line 1, as follows:

Framework 4

103 110 113
Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
TGG GGC CAG GGA GTC CTG GTC ACC GTC TCC TCA (SEQ ID NO: 3 – bases 391-423)

Please amend the captioned section beginning at page 50, line 3, as follows:

1. Cloning the light chain variable domain of primate monoclonal anti-human CD23 antibody 5E8 by PCR

The first PCR reaction of the light chain variable domain from FEE cDNA was carried out using a set of kappa early leader sequence primers and the 3' J region primer GE204 (SEQ ID NO: 13). (See primers for PCR of the kappa light chain variable domain of 5E8 in Tables 1-3 (SEQ ID NOs: 9-25)). A 420 base PCR product was obtained. The isolated 420 base PCR product was digested with Bgl II and BsiW I restriction endonucleases, cloned into the mammalian expression vector N5KG4P and sequenced using GE108 (SEQ ID NO: 29) and 377 (SEQ ID NO: 30) primers (which are contained in Table 4 (SEQ ID NOs: 26-35)): The mammalian expression vector N5KG4P is identical to the vector N5LG4P except it contains the human kappa light chain constant region in place of the human lambda light

24 30 34
Arg Ala Ser Gln Asp Ile Arg Tyr Tyr Leu Asn
AGG GCA AGT CAG GAC ATT AGG TAT TAT TTA AAT (SEQ ID NO: 5 – bases 136-168)

Please amend the captioned section beginning at page 51, line 21, as follows:

35		40		49										
Try	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
TGG	TAT	CAG	CAG	AAA	CCA	GGA	AAA	GCT	CCT	AAG	CTC	CTG	ATC	TAT

(SEQ ID NO: 5 – bases 169-213)

Please amend the captioned section beginning at page 51, line 25, as follows:

50 56
Val Ala Ser Ser Leu Gln Ser
GTT GCA TCC AGT TTG CAA AGT (SEQ ID NO: 5 – bases 214-234)

Please amend the captioned section beginning at page 51, line 29, as follows:

57	60										70				
Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	
GGG	GTC	CCA	TCA	AGG	TTC	AGC	GGC	AGT	GGA	TCT	GGG	ACA	GAG	TTC	
80															
Thr	Leu	Thr	Val	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	
ACT	CTC	ACC	GTC	AGC	AGC	CTG	CAG	CCT	GAA	GAT	TTT	GCG	ACT	TAT	
88															
Tyr	Cys														
TAC TGT (SEQ ID NO: 5 – bases 235-330)															

Please amend the paragraph beginning at page 53, line 6, as follows:

In order to determine the appropriate codon at 91, a third independent PCR was performed using the same primers as the second PCR (see above). The PCR product was again cloned into a TA vector and sequenced using Sp6 (SEQ ID NO: 26) and T7 (SEQ ID NO: 28) primers. The sequence was found to be identical to the heavy chain variable sequence obtained in the first PCR. Therefore, the TGC at position 91 in the second independent PCR product is apparently the result of an error introduced during PCR. This entire sequence of the heavy chain variable domain of primate monoclonal anti-human CD23 antibody 6G5 is presented below (~~SEQ ID NO: 4~~), as an alignment of the nucleotide sequence (SEQ ID NO: 7) and the encoded amino acid sequence (SEQ ID NO:8).

Please amend the captioned section beginning at page 53, line 18, as follows:

Heavy chain variable region of primate monoclonal antibody

anti-human CD23 5E8 Leader

Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Pro Leu Leu Lys
ATG GAG TTT GGG CTG AGC TGG GTT TTC CTT GTT CCT CTT TTG AAA
-1
Gly Val Gln Cys
GGT GTC CAG TGT (SEQ ID NO: 7 - bases 1-57)

Please amend the captioned section beginning at page 53, line 26, as follows:

Mature Protein (Numbering is Kabat)

Framework 1

1 10
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys Pro Gly
GAG GTG CAG CTG GTG GAG TCT GGG GGC GGC TTG GCA AAG CCT GGG
20 30
Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe Thr
GGG TCC CTG AGA CTC TCC TGC GCA GCC TCC GGG TTC AGG TTC ACC
(SEQ ID NO: 7 - bases 58-147)

Please amend the captioned section beginning at page 54, line 27, as follows:

CDR 3

95	100	101	
Leu	Thr	Thr	Gly Ser Asp Ser
TTG	ACT	ACA	GGG TCT GAC TCC (SEQ ID NO: 7- bases 358-378)

Please amend the captioned section beginning at page 55, line 1, as follows:

Framework 4

103	110	113	
Trp	Gly	Gln	Gly Val Leu Val Thr Val Ser Ser
TGG	GGC	CAG	GGA GTC CTG GTC ACC GTC TCC TCA (SEQ ID NO: 7 - bases 379-411)

Please amend the paragraph beginning at page 56, line 3, as follows:

A first PCR was done using N5KG4P + 5E8 as a template and a 3' primer (corresponding to codon 71 to 79) and which contains a mutation at codon 75 (AAC changed to AAG, Primer MB1654 (SEQ ID NO: 39), and a 5' primer at the beginning of the leader sequence (Primer MB1650) (SEQ ID NO: 36). (See PCR Primers Used for the Generation of a Glycosylation Mutant of the Heavy Chain Variable Region 5E8 set forth in Table 5 (SEQ ID NOs: 36-39)).

Please amend the paragraph beginning at page 56, line 11, as follows:

A second PCR was performed on the same template by using a 5' primer (corresponding to codon 71 to 79) containing the same mutation (Primer MB1653) (SEQ ID NO: 38) and a 3' primer from the end of framework 4 (Primer MB1651) (SEQ ID NO: 37) (See PCR Primers Used for the Generation of a Glycosylation Mutant of the Heavy Chain Variable Region of 5E8 in Table 5 (SEQ ID NOs: 36-39).)

Please amend the paragraph beginning at page 56, line 18, as follows:

These two PCR products were isolated and mixed in equal molar ratios. A third independent PCR was then carried out by using the mixture of the first and second PCR products as a template with a 5' primer used in the first PCR (MB1650) (SEQ ID NO: 36) and a 3' primer used in the second PCR (MP 1651) (SEQ ID NO: 37) (See PCP Primers Used for

the Generation of a Glycosylation Mutant of the Heavy Chain Variable Region in Table 5 (SEQ ID NOs: 36-39.) The PCR product obtained in third PCR was found to contain the heavy variable domain coding region of 5E8 wherein the asparagine 75 had been changed to lysine.

Please amend Tables 1-5 beginning at page 57, line 8 (in their entirety), as follows:

Table 1

Primers for PCR of the kappa light chain variable domain of 5E8

NAME	Light chain Vk -early leader 5' (Bgl II)	FAMILY
	-22 -21 -20 -19 -18 17 -16 -15 -14	
GE201	5' AT CAC <u>AGA TCT</u> CTC ACC ATG GAC ATG AGG GTC CCC GCT CAG 3'	1
	(SEQ ID NO: 5) (SEQ ID NO: 9)	
GE200	5' AT CAC <u>AGA TCT</u> CTC ACC ATG AGG CTC CCT GCT CAG 3'	2
	(SEQ ID NO: 6) (SEQ ID NO: 10)	
GE202	5' AT CAC <u>AGA TCT</u> CTC ACC ATG GAA (A/G)CC CCA GC(T/G) CAG 3'	3
	(SEQ ID NO: 7) (SEQ ID NO: 11)	
GE203	5' AT CAC <u>AGA TCT</u> CTC ACC ATG GTG TTG CAG ACC CAG GTC 3'	4
	(SEQ ID NO: 8) (SEQ ID NO: 12)	

Light chain Vk-3' primer (BsiW I)

	113 112 111 110 109 108 107 106 105 104 103
GE204	5' GG TGC AGC CAC <u>CGT AGC</u> TTT GAT (C/T)TC CA(G/C) CTT 3'
	(SEQ ID NO: 9) (SEQ ID NO: 13)

Table 2

Primers for PCR of the lambda light chain variable domain of 6G5

NAME	Light chain Vλ -early leader 5' (Bgl II)	FAMILY
	-20 -19 -18 -17 -16 -15	
744	5' AT CAC <u>AGA TCT</u> CTC ACC ATG (G/A)CC TG(G/C) TCC CCT CT 3'	1
	(SEQ ID NO: 10) (SEQ ID NO: 14)	
745	5' AT CAC <u>AGA TCT</u> CTC ACC ATG GCC TGG (A/G)CT C(T/C)G CT 3'	2

~~(SEQ ID NO: 11)~~ (SEQ ID NO: 15)

910 5' AT CAC AGA TCT CTC ACC ATG GC(A/C) TGG A(T/C)C CCT CTC 3' 3

~~(SEQ ID NO: 12)~~ (SEQ ID NO: 16)

Light chain V1-3' primer (Avr II)

110 109 108 107 106 105 104

926 5' (AC)10 CTT GGG CTG ACC TAG GAC GGT 3' ~~(SEQ ID NO: 13)~~ (SEQ ID NO: 17)

Table 3

**Primers for PCR of the heavy chain
variable domains from 6G5 and 5E8**

NAME	<u>Heavy chain-early leaders 5' (Sal I)</u>	<u>Family</u>
	-20 -19 -18 -17 -16 -15	
MB1503	5' GCG ACT AAG <u>TCG ACC</u> ATG GAC TGG ACC TGG 3'	1
	SEQ ID NO: 14 (SEQ ID NO: 18)	
MB1502	5' GCG ACT AAG <u>TCG ACC</u> ATG AAA CAC CTG TGG 3'	2, 4
	(SEQ ID NO: 15) (SEQ ID NO: 19)	
GE207	5' GCG ACT AAG <u>TCG ACC</u> ATG GAG TTT GGG CTG AGC 3'	3
	(SEQ ID NO: 16) (SEQ ID NO: 20)	
GE208	5' GCG ACT AAG <u>TCG ACC</u> ATG GGG TCA ACC GCC ATC 3'	5
	(SEQ ID NO: 17) (SEQ ID NO: 21)	
GE209	5' GCG ACT AAG <u>TCG ACC</u> ATG TCT GTC TCC TTC CTC 3'	6
	(SEQ ID NO: 18) (SEQ ID NO: 22)	

Heavy chain-3' primer (Nhe I)

120 119 118 117 116 115 114 113 112 111 110

GE244 5' GC CAG GGG GAA GAC CGA TGG GCC CTT GGT GCT AGC TGA GGA GAC GG 3'

~~SEQ ID NO: 19~~ (SEQ ID NO: 23)

GE210 5' GA TGG GCC CTT GGT GCT AGC TGA GGA GAC GG 3'

~~(SEQ ID NO: 20)~~ (SEQ ID NO: 24)

MB1533 5' GGT GCT AGC TGA GGA GAC GGT

109 108 107 106 105 104 103 101 100 99

GAC CAG GAC TCC CTG GCC CCA GAA GCC TAG 3'

~~(SEQ ID NO: 21)~~ (SEQ ID NO: 25)

Table 4
Sequencing Primers

Sp6 primer	5' AT TTA GGT GAC ACT ATA	3' (SEQ ID NO: 22) (SEQ ID NO: 26)
M13(-40) Forward Primer	5' GTT TTC CCA GTC ACG A	3' (SEQ ID NO: 23) (SEQ ID NO: 27)
T7 Promoter Primer	5' AT ATA CGA CTC ACT ATA GGG	3' (SEQ ID NO: 24) (SEQ ID NO: 28)
GE 108 Primer	5' CCG TCA GAT CGC CTG GAG ACG CCA	3' (SEQ ID NO: 25) (SEQ ID NO: 29)
377 Primer	5' GCA GTT CCA GAT TTC AAC TG	3' (SEQ ID NO: 26) (SEQ ID NO: 30)
607 PRIMER	5' CCA GGC CAC TGT CAC GGC TTC	3' (SEQ ID NO: 27) (SEQ ID NO: 31)
266 PRIMER	5' CAG AGC TGG GTA CGT CCT CA	3' (SEQ ID NO: 28) (SEQ ID NO: 32)
268 PRIMER	5' GCC CCC AGA GGT GCT CTT GG	3' (SEQ ID NO: 29) (SEQ ID NO: 33)
876 PRIMER	5' ACA CAG ACC CGT CGA CAT GG	3' (SEQ ID NO: 30) (SEQ ID NO: 34)
928 PRIMER	5' GCT CTC GGA GGT GCT CCT GG	3' (SEQ ID NO: 31) (SEQ ID NO: 35)

Table 5
PCR Primers Used for the Generation of a Glycosylation
Mutant of the Heavy Chain Variable Region of 5E8

	Sal I	-20 -19 -18 -17 -16	
MB 1650	5' ACA GAC CCG <u>TCG ACC</u> ATG GAG TTT GGG CTG	3' (SEQ ID NO: 32)	(SEQ ID NO: 36)
	Nhe I	118 117 116 115 114 113 112 111 110	
MB 1651	5' CCC CTT GGT <u>GCT AGC</u> TGA GGA GAC GGT	3' (SEQ ID NO: 33)	(SEQ ID NO: 37)
		71 72 73 74 75 76 77 78 79	
MB 1653	5' AGA GAG AAC GCC AAG AAC ACA CTG TTT	3' (SEQ ID NO: 34)	(SEQ ID NO: 38)

79 78 77 76 75 74 73 72 71
MB 1654 5' AAA CAG TGT GTT CTT GGC GTT CTC TCT 3' ~~(SEQ ID NO: 35)~~ (SEQ ID
NO: 39)

Please delete the sequence listing beginning at page 89 of the specification (in its entirety), which was amend on July 25, 2000, to include the sequence listing filed on that day, and in place thereof insert the sequence listing submitted herewith.

Amendments To The Claims

1-41. (Canceled)

ntly amended) A chimeric anti-human CD23 antibody wherein the light
n consists of the ~~variable domain~~ polypeptide encoded by nucleotides
D: 1, the heavy chain variable domain consists of the ~~variable domain~~
y ~~SEQ ID NO: 2~~ nucleotides 48-423 of SEQ ID NO:3, and the constant
tant region selected from the group consisting of human gamma-1 and
nt regions.

in pencil
-amendments
proposed by
examiner
06-28-04
JBM

chimeric 58

ly presented) The ^{chimeric} anti-human CD23 antibody of claim 42 wherein
n is a human gamma-1 constant region.

chimeric

... (Previously presented) The ^{chimeric} anti-human CD23 antibody of claim 42 wherein
the human constant region is a human gamma-3 constant region.

45. (Currently amended) A composition containing ~~an~~ ^{chimeric} the anti-human CD23
antibody according to claim 42 and a pharmaceutically acceptable carrier.

46. (Currently amended) A composition containing ~~an~~ ^{chimeric} the anti-human CD23
antibody according to claim 43 and a pharmaceutically acceptable carrier.

47. (Currently amended) A composition containing ~~an~~ ^{chimeric} the anti-human CD23
antibody according to claim 44 and a pharmaceutically acceptable carrier.

48. (Currently amended) A chimeric anti-human CD23 antibody wherein the light
chain variable domain consists of the ~~variable domain~~ polypeptide encoded by ~~SEQ ID NO: 3~~
nucleotides 67-387 of SEQ ID NO: 5, the heavy chain variable domain consists of the
~~variable domain~~ polypeptide encoded by ~~[nucleotides 58-411]~~ ^{chimeric} of SEQ ID NO: 4 nucleotides
58-411 of SEQ ID NO: 7, and the constant region is a human constant region selected from
the group consisting of a human gamma-1 constant region and a human gamma-3 constant
region.

49. (Currently amended) A chimeric anti-human CD23 antibody wherein the light chain variable domain consists of the ~~variable domain~~ polypeptide encoded by ~~SEQ ID NO: 3~~ nucleotides 67-387 of SEQ ID NO: 5 and the heavy chain variable domain consists of the ~~variable domain~~ polypeptide encoded by ~~SEQ ID NO: 4~~ nucleotides 58-411 of SEQ ID NO: 7 with the exception that the asparagine codon encoded by nucleotides 289-291 of ~~SEQ ID NO:~~

[4] ~~SEQ ID NO: 7~~ is replaced with a lysine codon.

50. (Currently amended) The ^{chimeric} anti-human CD23 antibody according to claim 48 ~~which comprises wherein the human constant region is~~ a human gamma-1 constant region.

51. (Currently amended) The ^{chimeric} anti-human CD23 antibody according to claim 48 ~~which comprises wherein the human constant region is~~ a human gamma-3 constant region.

52. (Currently amended) The ^{chimeric} anti-human CD23 antibody according to claim 49 ~~which comprises wherein the human constant region is~~ gamma-1 constant region.

53. (Previously presented) The ^{chimeric} anti-human CD23 antibody according to claim 49 which comprises a human gamma-3 constant region.

54. (Currently amended) A composition comprising ~~an~~ ^{chimeric} the anti-human CD23 antibody according to claim 48 and a pharmaceutically acceptable carrier.

55. (Currently amended) A composition comprising ~~an~~ ^{chimeric} the anti-human CD23 antibody according to claim 49 and a pharmaceutically acceptable carrier.

56. (Currently amended) A composition comprising ~~an~~ ^{chimeric} the anti-human CD23 antibody according to claim 50 and a pharmaceutically acceptable carrier.

57. (Currently amended) A composition comprising ~~an~~ ^{chimeric} the anti-human CD23 antibody according to claim 51 and a pharmaceutically acceptable carrier.

58. (Currently amended) A composition comprising ~~an~~ the ^{chimeric} anti-human CD23 antibody according to claim 52 and a pharmaceutically acceptable carrier.

59. (Currently amended) A composition comprising ~~an~~ the ^{chimeric} anti-human CD23 antibody according to claim 53 and a pharmaceutically acceptable carrier.

60. (Canceled)

61. (Previously presented) The composition of claim 45, which composition is a pharmaceutical composition.

62. (Previously presented) The composition of claim 46, which composition is a pharmaceutical composition.

63. (Previously presented) The composition of claim 47, which composition is a pharmaceutical composition.

64. (Previously presented) The composition of claim 54, which composition is a pharmaceutical composition.

65. (Previously presented) The composition of claim 55, which composition is a pharmaceutical composition.

66. (Previously presented) The composition of claim 56, which composition is a pharmaceutical composition.

67. (Previously presented) The composition of claim 57, which composition is a pharmaceutical composition.

68. (Previously presented) The composition of claim 58, which composition is a pharmaceutical composition.

69. (Previously presented) The composition of claim 59, which composition is a pharmaceutical composition.

70-73. (Canceled)

REMARKS

Status Summary

The request for continued examination (RCE) filed on October 21, 2003, has been entered. Claims 42-59, 61-69, and 71-73 are pending in the application and were examined. Claims 42-59 and 54-59 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. A notice to comply with requirements for applications containing nucleic acid and amino acid sequences was issued together with the official action.

Claims 42, 45-52, are amended and claims 71-73 are canceled. A substitute sequence listing, including a paper copy and a computer-readable copy, and the requisite statement pursuant to 37 C.F.R. 1.821(f) are submitted herewith. The specification and claims are amended to use sequence identifiers as in the substitute sequence listing and to incorporate language suggested by the examiner with respect to 35 U.S.C. § 112, second paragraph. Reconsideration in view of the claim amendments and following remarks is respectfully requested.

Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

Claims 42-59, 61-69 and 71-73 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The rejection is based on noted informalities in the claims.

Claims 42, 45-52 are amended to incorporate language substantially as suggested by the examiner. With respect to claims 42, 48, and 49, the second mention of "variable domain" has been replaced with language specifying the nucleotides comprising the variable domain to clarify that leader sequence of each of SEQ ID NOs: 1, 3, 5, and 7 is not included. Claims 71, 72, and 73 are canceled as duplicative of claims 42, 48, and 49, respectively. Claims 43-44, 53-59, 61-69, and 71-73 depend from the amended claims and are believed to fully comply with the requirements of 35 U.S.C. § 112, second paragraph. Based thereon, withdrawal of the rejection is respectfully requested.

Notice to Comply with Requirements for Applications

Containing Nucleic Acid and Amino Acid Sequences

A notice to comply with requirements for applications containing nucleic acid and amino acid sequences was issued together with the official action. The previously submitted sequence fails to comply with the relevant rules because the computer-readable format copy

of SEQ ID NO:4 has only 354 nucleotides whereas the paper copy shows SEQ ID NO:4 as consisting of 411 nucleotides. The computer-readable format copy erroneously included a truncated sequence.

A substitute sequence listing, including a paper copy and a computer-readable copy, and the requisite statement pursuant to 37 C.F.R. 1.821(f) are submitted herewith. The substitute sequence listing includes a total of 39 sequences whereas the amendment filed July 25, 2000, includes a total of 35 sequences. The 4 additional sequences arise due to the separate listing of the nucleotide and amino acid sequences of former SEQ ID NOs:1-4, which now correspond to the nucleotide sequences of SEQ ID NOs: 1, 3, 5, and 7, and the amino acid sequences of SEQ ID NOs:2, 4, 6, and 8. In addition, nucleotides 118-120 of the 6G5 heavy chain variable region, which were identified as "TGG" encoding tryptophan (Trp) in SEQ ID NO:4 of the sequence listing filed July 25, 2000, are identified as "TCC" encoding serine (Ser) in SEQ ID NO:7 of the substitute sequence listing submitted herewith. The amendment is made to correct a typographical error in preparation of the sequence listing. Support for the amendment can be found in the originally filed application at the last line of page 53 and the first line of page 54. No new matter is added.

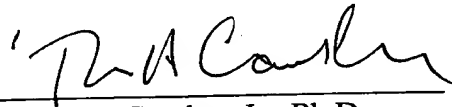
The specification is amended to insert the instant sequence listing in place of the previously filed sequence listing. The specification and claims are amended to use sequence modifiers as in the substitute sequence listing submitted herewith.

Conclusion

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a notice to that effect is earnestly solicited. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

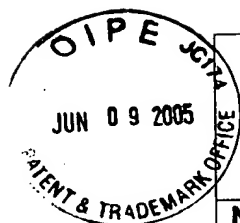
Respectfully submitted,

PILLSBURY WINTHROP LLP



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Notice to Comply

Application No.

Applicant(s)

Examiner
Phuong N. Huynh

Art Unit
1644

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☒ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: It is noted that the computer copy of SEQ ID NO: 4 has only 354 nucleotides. Both computer and paper copy of the sequence listing of SEQ ID NO: 4 should have been 411 nucleotides.

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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U.S. Application No. 09/019,441
Attorney Ref. No. 037003-0275470



<110> REFF, MITCHELL E.
KLOETZER, WILLIAM S.
NAKAMURA, TAKEHIKO

<120> GAMMA-1 AND GAMMA-3 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES AND USE
THEREOF AS THERAPEUTICS

<130> 037003-0275470

<140> 09/019,441

<141> 1998-02-05

<150> 08/803,085

<151> 1997-02-20

<160> 39

<170> PatentIn Ver. 2.1

<210> 1

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World Monkey (macaque); leader sequence is an artificial sequence to
facilitate cloning

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<222> (1)..(57)

<223> leader sequence

<220>

<221> mat_peptide

<222> (58)..(390)

<220>

<221> CDS

<222> (1)..(390)

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Met Ala Trp Thr Leu Leu Leu Val Thr Leu Leu Thr Gln Gly Thr Gly	
-15 -10 -5	

tcc tgg gct cag tct gcc ccg act cag cct ccc tct gtg tct ggg tct	96
Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser	
-1 1 5 10	

cct gga cag tcg gtc acc atc tcc tgc act gga acc agc gat gac gtt	144
Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val	
15 20 25	

ggt ggt tat aac tat gtc tcc tgg tac caa cac cac cca ggc aaa gcc 192
Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
30 35 40 45

ccc aaa ctc atg att tat gat gtc gct aag cgg gcc tca ggg gtc tct 240
Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
50 55 60

gat cgc ttc tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc 288
Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
65 70 75

tct ggg ctc cag gct gag gac gag gct gat tat tac tgt tgt tca tat 336
Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
80 85 90

aca acc agt agc act ttg tta ttc gga aga ggg acc cgg ttg acc gtc 384
Thr Thr Ser Ser Thr Leu Leu Phe Gly Arg Gly Thr Arg Leu Thr Val
95 100 105

cta ggt 390
Leu Gly
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<210> 2

<211> 130

<212> PRT

<213> Artificial Sequence

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<400> 2

Met Ala Trp Thr Leu Leu Leu Val Thr Leu Leu Thr Gln Gly Thr Gly
-15 -10 -5

Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser
-1 1 5 10

Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val
15 20 25

Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
30 35 40 45

Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
50 55 60

Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
65 70 75

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
80 85 90

Thr Thr Ser Ser Thr Leu Leu Phe Gly Arg Gly Thr Arg Leu Thr Val
95 100 105

Leu Gly
110

<210> 3
<211> 423
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<223> leader sequence

<220>
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<222> (58)..(423)

<220>
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atg aaa cac ctg tgg ttc ttc ctc ctc ctg gtg gca gct ccc aga tgg	48
Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp	
-15 -10 -5	
gtc ctg tcc cag ctg cag ctg cag gag tgc ggc cca gga gtg gtg aag	96
Val Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys	
-1 1 5 10	
cct tgc gag acc ctg tcc ctc acc tgc gct gtc tct ggt ggc tct gtc	144
Pro Ser Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val	
15 20 25	
agc agt agt aac tgg tgg acc tgg atc cgc cag ccc cca ggg aag gga	192
Ser Ser Ser Asn Trp Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly	
30 35 40 45	
ctg gag tgg att gga cgt atc tct ggt agt ggt ggg gcc acc aac tac	240
Leu Glu Trp Ile Gly Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr	
50 55 60	
aac ccg tcc ctc aag agt cga gtc atc att tca caa gac acg tcc aag	288
Asn Pro Ser Leu Lys Ser Arg Val Ile Ile Ser Gln Asp Thr Ser Lys	
65 70 75	
aac cag ttc tcc ctg aac ctg aac tct gtg acc gcc gcg gac acg gcc	336
Asn Gln Phe Ser Leu Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala	
80 85 90	
gtg tat tac tgt gcc aga gat tgg gcc caa ata gct gga aca acg cta	384
Val Tyr Tyr Cys Ala Arg Asp Trp Ala Gln Ile Ala Gly Thr Thr Leu	
95 100 105	

ggc ttc tgg ggc cag gga gtc ctg gtc acc gtc tcc tca
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

423

<210> 4
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Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
-15 -10 -5
Val Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys
-1 1 5 10
Pro Ser Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val
15 20 25
Ser Ser Ser Asn Trp Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly
30 35 40 45
Leu Glu Trp Ile Gly Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr
50 55 60
Asn Pro Ser Leu Lys Ser Arg Val Ile Ile Ser Gln Asp Thr Ser Lys
65 70 75
Asn Gln Phe Ser Leu Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala
80 85 90
Val Tyr Tyr Cys Ala Arg Asp Trp Ala Gln Ile Ala Gly Thr Thr Leu
95 100 105
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

<210> 5
<211> 387
<212> DNA
<213> Artificial Sequence

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<223> leader sequence

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<222> (67)..(387)

<220>
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Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp	
-20 -15 -10	
ctc cca ggt gcc aga tgt gac atc cag atg acc cag tct cca tct tcc	96
Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser	
-5 -1 1 5 10	
ctg tct gca tct gta ggg gac aga gtc acc atc act tgc agg gca agt	144
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser	
15 20 25	
cag gac att agg tat tat tta aat tgg tat cag cag aaa cca gga aaa	192
Gln Asp Ile Arg Tyr Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys	
30 35 40	
gct cct aag ctc ctg atc tat gtt gca tcc agt ttg caa agt ggg gtc	240
Ala Pro Lys Leu Leu Ile Tyr Val Ala Ser Ser Leu Gln Ser Gly Val	
45 50 55	
cca tca agg ttc agc ggc agt gga tct ggg aca gag ttc act ctc acc	288
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr	
60 65 70	
gtc agc agc ctg cag cct gaa gat ttt gcg act tat tac tgt cta cag	336
Val Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln	
75 80 85 90	
gtt tat agt acc cct cgg acg ttc ggc caa ggg acc aag gtg gaa atc	384
Val Tyr Ser Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile	
95 100 105	
aaa	387
Lys	

<210> 6
<211> 129
<212> PRT
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<400> 6

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
-20 -15 -10
Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser

-5	-1	1	5	10
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser	15	20	25	
Gln Asp Ile Arg Tyr Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys	30	35	40	
Ala Pro Lys Leu Leu Ile Tyr Val Ala Ser Ser Leu Gln Ser Gly Val	45	50	55	
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr	60	65	70	
Val Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln	75	80	85	90
Val Tyr Ser Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile	95	100	105	

Lys

<210> 7
<211> 411
<212> DNA
<213> Artificial Sequence

<220>
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<223> leader sequence

<220>
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Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Pro Leu Leu Lys Gly	
-15 -10 -5	
gtc cag tgt gag gtg cag ctg gtg gag tct ggg ggc ggc ttg gca aag	96
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys	
-1 1 5 10	
cct ggg ggg tcc ctg aga ctc tcc tgc gca gcc tcc ggg ttc agg ttc	144
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe	
15 20 25	


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acc ttc aat aac tac tac atg gac tgg gtc cgc cag gct cca ggg cag 192
Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
30 35 40 45

ggg ctg gag tgg gtc tca cgt att agt agt agt ggt gat ccc aca tgg 240
Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
50 55 60

tac gca gac tcc gtg aag ggc aga ttc acc atc tcc aga gag aac gcc 288
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
65 70 75

aac aac aca ctg ttt ctt caa atg aac agc ctg aga gct gag gac acg 336
Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
80 85 90

gct gtc tat tac tgt gcg agc ttg act aca ggg tct gac tcc tgg ggc 384
Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
95 100 105

cag gga gtc ctg gtc acc gtc tcc tca 411
Gln Gly Val Leu Val Thr Val Ser Ser
110 115

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<210> 8
<211> 137
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<400> 8

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Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Pro Leu Leu Lys Gly
-15 -10 -5

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys
-1 1 5 10

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe
15 20 25

Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
30 35 40 45

Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
50 55 60

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
65 70 75

Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
80 85 90

Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
95 100 105

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Gln Gly Val Leu Val Thr Val Ser Ser
110 115

<210> 9
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<220>
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<210> 10
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
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<400> 10
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<210> 11
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<400> 11
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<210> 12
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<400> 12
atcacagatc tctcaccatg gtgttcgaga cccaggtc 38

<210> 13
<211> 32
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<220>

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<400> 13

ggtgcagcca ccgtagcttt gatytccasc tt

32

<210> 14

<211> 34

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<220>

<223> Description of Artificial Sequence: Primer

<400> 14

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34

<210> 15

<211> 34

<212> DNA

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<400> 15

atcacagatc tctcaccatg gcctggrctc ygct

34

<210> 16

<211> 35

<212> DNA

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<210> 17

<211> 21

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<400> 17

cttgggctga cctaggacgg t

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<210> 18

<211> 30

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<400> 18

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<210> 19
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<210> 20
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gcgactaagt cgaccatggg gtcaaccgcc atc 33

<210> 22
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<400> 23

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<210> 24
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<400> 25

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<210> 26
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<400> 26

atttagtgta cactata 17

<210> 27
<211> 16
<212> DNA
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<223> Description of Artificial Sequence: Primer

<400> 27

gttttcccag tcacga

16

<210> 28

<211> 20

<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Primer

<400> 28

atatacgact cactataggg

20

<210> 29

<211> 24

<212> DNA

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<400> 29

ccgtcagatc gcctggagac gcca

24

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<212> DNA

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20

<210> 33

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<210> 34

<211> 20

<212> DNA

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20

<210> 35

<211> 20

<212> DNA

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<400> 35

gctctcggag gtgctcctgg

20

<210> 36

<211> 30

<212> DNA

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30

<210> 37
<211> 27
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<400> 38

agagagaacg ccaagaacac actgttt

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<210> 39
<211> 27
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<400> 39

aaacagtgtg ttcttggcgt tctctct

27

SEQUENCE LISTING

<110> REFF, MITCHELL E.
KLOETZER, WILLIAM S.
NAKAMURA, TAKEHIKO

<120> GAMMA-1 AND GAMMA-3 ANTI-HUMAN CD23 MONOCLONAL ANTIBODIES AND USE
THEREOF AS THERAPEUTICS

<130> 037003-0275470

<140> 09/019,441

<141> 1998-02-05

<150> 08/803,085

<151> 1997-02-20

<160> 39

<170> PatentIn Ver. 2.1

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World Monkey (macaque); leader sequence is an artificial sequence to
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<223> leader sequence

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atg gcc tgg act ctg ctc ctc gtc acc ctc ctc act cag ggc aca gga	48
Met Ala Trp Thr Leu Leu Leu Val Thr Leu Leu Thr Gln Gly Thr Gly	
-15 -10 -5	

tcc tgg gct cag tct gcc ccg act cag cct ccc tct gtg tct ggg tct	96
Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser	
-1 1 5 10	

cct gga cag tcg gtc acc atc tcc tgc act gga acc agc gat gac gtt	144
Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val	
15 20 25	

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ggt ggt tat aac tat gtc tcc tgg tac caa cac cac cca ggc aaa gcc 192
Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
30 35 40 45

ccc aaa ctc atg att tat gat gtc gct aag cgg gcc tca ggg gtc tct 240
Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
50 55 60

gat cgc ttc tct ggc tcc aag tct ggc aac acg gcc tcc ctg acc atc 288
Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
65 70 75

tct ggg ctc cag gct gag gac gag gct gat tat tac tgt tgt tca tat 336
Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
80 85 90

aca acc agt agc act ttg tta ttc gga aga ggg acc cgg ttg acc gtc 384
Thr Thr Ser Ser Thr Leu Leu Phe Gly Arg Gly Thr Arg Leu Thr Val
95 100 105

cta ggt 390
Leu Gly
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<210> 2
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<400> 2

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Met Ala Trp Thr Leu Leu Leu Val Thr Leu Leu Thr Gln Gly Thr Gly
-15 -10 -5

Ser Trp Ala Gln Ser Ala Pro Thr Gln Pro Pro Ser Val Ser Gly Ser
-1 1 5 10

Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Asp Asp Val
15 20 25

Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln His His Pro Gly Lys Ala
30 35 40 45

Pro Lys Leu Met Ile Tyr Asp Val Ala Lys Arg Ala Ser Gly Val Ser
50 55 60

Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
65 70 75

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Cys Ser Tyr
80 85 90

Thr Thr Ser Ser Thr Leu Leu Phe Gly Arg Gly Thr Arg Leu Thr Val
95 100 105

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Leu Gly
110

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<223> leader sequence

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<222> (58)..(423)

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<222> (1)..(423)

<400> 3

atg	aaa	cac	ctg	tgg	ttc	ttc	ctc	ctc	ctg	gtg	gca	gct	ccc	aga	tgg	48
Met	Lys	His	Leu	Trp	Phe	Phe	Leu	Leu	Leu	Val	Ala	Ala	Pro	Arg	Trp	
				-15					-10					-5		
gtc	ctg	tcc	cag	ctg	cag	ctg	cag	gag	tcg	ggc	cca	gga	gtg	gtg	aag	96
Val	Leu	Ser	Gln	Leu	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Val	Val	Lys	
	-1	1					5					10				
cct	tcg	gag	acc	ctg	tcc	ctc	acc	tgc	gct	gtc	tct	ggt	ggc	tct	gtc	144
Pro	Ser	Glu	Thr	Leu	Ser	Leu	Thr	Cys	Ala	Val	Ser	Gly	Gly	Ser	Val	
	15					20					25					
agc	agt	agt	aac	tgg	tgg	acc	tgg	atc	cgc	cag	ccc	cca	ggg	aag	gga	192
Ser	Ser	Ser	Asn	Trp	Trp	Thr	Trp	Ile	Arg	Gln	Pro	Pro	Gly	Lys	Gly	
	30				35				40					45		
ctg	gag	tgg	att	gga	cgt	atc	tct	ggt	agt	ggt	ggg	gcc	acc	aac	tac	240
Leu	Glu	Trp	Ile	Gly	Arg	Ile	Ser	Gly	Ser	Gly	Gly	Ala	Thr	Asn	Tyr	
				50				55						60		
aac	ccg	tcc	ctc	aag	agt	cga	gtc	atc	att	tca	caa	gac	acg	tcc	aag	288
Asn	Pro	Ser	Leu	Lys	Ser	Arg	Val	Ile	Ile	Ser	Gln	Asp	Thr	Ser	Lys	
			65				70					75				
aac	cag	ttc	tcc	ctg	aac	ctg	aac	tct	gtg	acc	gcc	gcg	gac	acg	gcc	336
Asn	Gln	Phe	Ser	Leu	Asn	Leu	Asn	Ser	Val	Thr	Ala	Ala	Asp	Thr	Ala	
		80				85					90					
gtg	tat	tac	tgt	gcc	aga	gat	tgg	gcc	caa	ata	gct	gga	aca	acg	cta	384
Val	Tyr	Tyr	Cys	Ala	Arg	Asp	Trp	Ala	Gln	Ile	Ala	Gly	Thr	Thr	Leu	
	95					100					105					

ggc ttc tgg ggc cag gga gtc ctg gtc acc gtc tcc tca
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

423

<210> 4
<211> 141
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<400> 4

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
-15 -10 -5
Val Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Val Val Lys
-1 1 5 10
Pro Ser Glu Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Val
15 20 25
Ser Ser Ser Asn Trp Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly
30 35 40 45
Leu Glu Trp Ile Gly Arg Ile Ser Gly Ser Gly Gly Ala Thr Asn Tyr
50 55 60
Asn Pro Ser Leu Lys Ser Arg Val Ile Ile Ser Gln Asp Thr Ser Lys
65 70 75
Asn Gln Phe Ser Leu Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Ala
80 85 90
Val Tyr Tyr Cys Ala Arg Asp Trp Ala Gln Ile Ala Gly Thr Thr Leu
95 100 105
Gly Phe Trp Gly Gln Gly Val Leu Val Thr Val Ser Ser
110 115 120

<210> 5
<211> 387
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<220>
<221> misc_feature
<222> (1)..(66)
<223> leader sequence

<220>

<221> mat_peptide
<222> (67)..(387)

<220>
<221> CDS
<222> (1)..(387)

<400> 5

atg gac atg agg gtc ccc gct cag ctc ctg ggg ctc ctt ctg ctc tgg	48
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Trp	
-20 -15 -10	
ctc cca ggt gcc aga tgt gac atc cag atg acc cag tct cca tct tcc	96
Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser	
-5 -1 1 5 10	
ctg tct gca tct gta ggg gac aga gtc acc atc act tgc agg gca agt	144
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser	
15 20 25	
cag gac att agg tat tat tta aat tgg tat cag cag aaa cca gga aaa	192
Gln Asp Ile Arg Tyr Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys	
30 35 40	
gct cct aag ctc ctg atc tat gtt gca tcc agt ttg caa agt ggg gtc	240
Ala Pro Lys Leu Leu Ile Tyr Val Ala Ser Ser Leu Gln Ser Gly Val	
45 50 55	
cca tca agg ttc agc ggc agt gga tct ggg aca gag ttc act ctc acc	288
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr	
60 65 70	
gtc agc agc ctg cag cct gaa gat ttt gcg act tat tac tgt cta cag	336
Val Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln	
75 80 85 90	
gtt tat agt acc cct cgg acg ttc ggc caa ggg acc aag gtg gaa atc	384
Val Tyr Ser Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile	
95 100 105	
aaa	387
Lys	

<210> 6
<211> 129
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<400> 6

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
-20 -15 -10
Leu Pro Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser

-5	-1	1		5		10									
Leu	Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser
				15					20					25	
Gln	Asp	Ile	Arg	Tyr	Tyr	Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys
			30					35					40		
Ala	Pro	Lys	Leu	Leu	Ile	Tyr	Val	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val
		45					50					55			
Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr
	60					65					70				
Val	Ser	Ser	Leu	Gln	Pro	Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Leu	Gln
	75				80					85					90
Val	Tyr	Ser	Thr	Pro	Arg	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile
				95					100					105	

Lys

<210> 7
<211> 411
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<220>
<221> misc_feature
<222> (1)..(57)
<223> leader sequence

<220>
<221> mat_peptide
<222> (58)..(411)

<220>
<221> CDS
<222> (1)..(411)

<400> 7

atg	gag	ttt	ggg	ctg	agc	tgg	gtt	ttc	ctt	gtt	cct	ctt	ttg	aaa	ggt	48
Met	Glu	Phe	Gly	Leu	Ser	Trp	Val	Phe	Leu	Val	Pro	Leu	Leu	Lys	Gly	
				-15				-10						-5		
gtc	cag	tgt	gag	gtg	cag	ctg	gtg	gag	tct	ggg	ggc	ggc	ttg	gca	aag	96
Val	Gln	Cys	Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Ala	Lys	
	-1	1					5					10				
cct	ggg	ggg	tcc	ctg	aga	ctc	tcc	tgc	gca	gcc	tcc	ggg	ttc	agg	ttc	144
Pro	Gly	Gly	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Arg	Phe	
	15					20					25					

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acc ttc aat aac tac tac atg gac tgg gtc cgc cag gct cca ggg cag 192
Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
30 35 40 45

ggg ctg gag tgg gtc tca cgt att agt agt agt ggt gat ccc aca tgg 240
Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
50 55 60

tac gca gac tcc gtg aag ggc aga ttc acc atc tcc aga gag aac gcc 288
Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
65 70 75

aac aac aca ctg ttt ctt caa atg aac agc ctg aga gct gag gac acg 336
Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
80 85 90

gct gtc tat tac tgt gcg agc ttg act aca ggg tct gac tcc tgg ggc 384
Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
95 100 105

cag gga gtc ctg gtc acc gtc tcc tca 411
Gln Gly Val Leu Val Thr Val Ser Ser
110 115

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<210> 8

<211> 137

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Mature peptide is derived from Old World Monkey (macaque); leader sequence is an artificial sequence to facilitate cloning

<400> 8

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Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Pro Leu Leu Lys Gly
-15 -10 -5

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Lys
-1 1 5 10

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Arg Phe
15 20 25

Thr Phe Asn Asn Tyr Tyr Met Asp Trp Val Arg Gln Ala Pro Gly Gln
30 35 40 45

Gly Leu Glu Trp Val Ser Arg Ile Ser Ser Ser Gly Asp Pro Thr Trp
50 55 60

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala
65 70 75

Asn Asn Thr Leu Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
80 85 90

Ala Val Tyr Tyr Cys Ala Ser Leu Thr Thr Gly Ser Asp Ser Trp Gly
95 100 105

```

Gln Gly Val Leu Val Thr Val Ser Ser
110 115

<210> 9
<211> 41
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 9
atcacagatc tctcaccatg gacatgaggg tccccgctca g 41

<210> 10
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 10
atcacagatc tctcaccatg aggotccctg ctcatg 35

<210> 11
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 11
atcacagatc tctcaccatg gaarccccag ckcatg 35

<210> 12
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 12
atcacagatc tctcaccatg gtgttgacaga cccaggtc 38

<210> 13
<211> 32
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 13

ggtgcagcca ccgtagcttt gatytcasc tt

32

<210> 14

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 14

atcacagatc tctcaccatg rccgtgstccc ctct

34

<210> 15

<211> 34

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 15

atcacagatc tctcaccatg gcctgggrctc ygct

34

<210> 16

<211> 35

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 16

atcacagatc tctcaccatg gcmtggaycc ctctc

35

<210> 17

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 17

cttgggctga cctaggacgg t

21

<210> 18

<211> 30

<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 18

gcgactaagt cgaccatgga ctggacctgg

30

<210> 19
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 19

gcgactaagt cgaccatgaa acacctgtgg

30

<210> 20
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 20

gcgactaagt cgaccatgga gtttgggctg agc

33

<210> 21
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 21

gcgactaagt cgaccatggg gtcaaccgcc atc

33

<210> 22
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 22

gcgactaagt cgaccatgtc tgtctccttc etc

33

<210> 23
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 23

gccaggggga agaccgatgg gcccttggtg ctagctgagg agacgg

46

<210> 24
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 24

gatgggccct tgggtgctagc tgaggagacg g

31

<210> 25
<211> 51
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 25

ggtgctagct gaggagacgg tgaccaggac tccctggccc cagaagccta g

51

<210> 26
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 26

atttaggtga cactata

17

<210> 27
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 27

gttttcccag tcacga

16

<210> 28

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 28

atatacgact cactataggg

20

<210> 29

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 29

ccgtcagatc gcctggagac gcca

24

<210> 30

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 30

gcagttccag atttcaactg

20

<210> 31

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 31

ccaggccact gtcacggctt c

21

<210> 32

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 32

cagagctggg tacgtcctca

20

<210> 33

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 33

gccccagag gtgctcttgg

20

<210> 34

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 34

acacagaccg gtcgacatgg

20

<210> 35

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 35

gctctcggag gtgctcctgg

20

<210> 36

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Primer

<400> 36

acagaccggt cgaccatgga gtttgggctg

30

<210> 37
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 37

ccccttggtg ctagctgagg agacggt

27

<210> 38
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 38

agagagaacg ccaagaacac actgttt

27

<210> 39
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Primer

<400> 39

aaacagtgtg ttcttggcgt tctctct

27